Multi-sensor and real-time analyses Multi-Organ-On-a-Chip to study glucose homeostasis for diabetology

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Diabetes is the result of a deficiency in the glucose homeostasis (i.e. the control of blood glucose levels) leading to chronic hyperglycaemia (too much glucose in the blood). This physiological process involves crosstalk between the following organs mainly: the pancreas, the muscles, the liver and the adipose tissues (fat). To better understand these interactions and their deregulations upon pathogenic conditions, Multi-Organ-On-Chip (MOOC) represents a promising new approach. In these microdevices, different cell types are cultured in a microfluidic chip under flow in a controlled environment. The cells behavior is generally monitored through off-line measurements. My PhD work aims at establishing and validating a MOOC composed of pancreatic islets, which release the hormones regulating the glycaemia, and skeletal muscles, the main 'consumers' of glucose in the body. The activity of these cells will be monitored by several sensors achieving in-line monitoring and analysis.

To this end, the MOOC of this work involves both pancreatic islets and myotubes, which are skeletal muscle cells. On one hand, the engineering challenges are to design the microfluidic chip with its embedded sensors and electronics for control and recording. The microfluidic chip substrate is a commercial Micro-Electrode Array (MEA) that monitors non-invasively the electrical activity of the cells. The MEA will be in association with electrochemical glucose and lactate sensors in contact with the microfluidic flow thanks to a flow cell. On the other hand, the biological challenges are to determine the optimal cell culture conditions and the scaling (i.e. proportion between islets and myotubes). A multiphysics simulation software (COMSOL) is used prior to experimental validations.

The chip design has been validated with COMSOL to limit shear stress (mechanical stress for the cells under flow) that could affect cell function and lead to their detachment from the substrate. The chip layout has been assessed thanks to a prototype, and has validated the sealing and microfluidic flow. A first version of the recording electronic board was developed to determine the glucose concentration range where the glucose sensor is usable. A co-culture medium has been identified and shows to improve myotube lifetime.

Simulations are also carried to investigate the scaling needed, by modeling glucose, hormones and oxygen dynamics in the chip according to the cell number, chip size, and the flow rate. The glucose and lactate sensors have still to be characterized and the optimal coating procedure remains to be found, in view of the first functional assessments in real-time. The demonstration of the co-culture medium is carried out.